

ORIGINAL ARTICLE

Cerebral Oxygenation During Hypoxia and Resuscitation by Using Near-infrared Spectroscopy in Newborn Piglets

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Background: Hypoxic events and cardiac arrest may cause brain damage in critical infants. This study investigated cerebral tissue oxygenation and oxygen extraction in a piglet model of hypoxic events, cardiac arrest and effects of resuscitation.

Methods: For the hypoxia experiment, anesthetized newborn piglets were randomized to a hypoxia group ($n=8$) with decreasing ventilatory rate to 0, and a control group ($n=8$) with no hypoxic conditions. Regional cerebral tissue oxygen saturation ($rScO_2$, detected by near-infrared spectroscopy) and oxygen saturation were recorded every 5 minutes for 100 minutes. Fractional cerebral tissue oxygen extraction (FTOE) was calculated as $(\text{arterial oxygen saturation } [SaO_2] - rScO_2) / SaO_2$. For the resuscitation experiment, animals were grouped as hypoxia-no CPR ($n=4$), control-no CPR ($n=4$), and control-CPR ($n=4$) after cardiac arrest. Standard cardiopulmonary resuscitation (CPR) was performed on the control-CPR group and observed for 30 minutes.

Results: Immediate and significant changes in $rScO_2$, and gradual changes in FTOE were observed during the hypoxia experiment. In the resuscitation experiment, no significant differences in $rScO_2$ were found between groups. However, the highest FTOE was observed in the control-CPR group.

Conclusion: Noninvasive monitoring of $rScO_2$ and evaluating FTOE changes during hypoxia and resuscitation may help clinicians evaluate brain tissue oxygenation and viability. [*J Chin Med Assoc* 2007;70(2):47–55]

Key Words: brain, hypoxia, near-infrared spectroscopy, piglet, resuscitation

Introduction

Hypoxic events, bradycardia and cardiac arrest are common critical conditions in pediatric and neonatal intensive care. Infants experiencing these conditions are likely to suffer brain tissue hypoxic insults. Oxygen supply, ventilatory care and resuscitation have been performed on these critical infants. However, some infants may still experience neurologic complications in the form of seizures, impaired cognition, developmental delay, cerebral palsy, or even death.^{1–4} A noninvasive method to monitor brain tissue oxygenation and oxygen extraction may be helpful for evaluating brain tissue damage in these critical infants.

Near-infrared spectroscopy (NIRS) is a noninvasive optical technology to monitor and reliably estimate changes in tissue oxygenation,^{5–11} and has been increasingly used to evaluate brain tissue oxygenation in infants.^{4,12–16} Decreased cerebral hemoglobin oxygenation has been observed in neonates at high risk of hypoxic-ischemic brain damage by using NIRS.^{12–15,17} However, increased regional cerebral oxygen saturation ($rScO_2$) and decreased fractional cerebral tissue oxygen extraction (FTOE) 24 hours after birth have been observed in neonates with severe birth asphyxia and adverse outcome.⁴ Therefore, a single $rScO_2$ value may not fully reflect brain damage in critical neonates.

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Our hypothesis was that rScO₂ and FTOE could be significantly influenced by hypoxic conditions, cardiac arrest, and therapeutic interventions including inspired oxygen and cardiopulmonary resuscitation (CPR) in neonatal infants. Therefore, we designed this study to investigate the changes in brain tissue oxygenation and oxygen extraction in newborn piglets with hypoxic events or cardiac arrest by using NIRS monitoring and calculating FTOE.

Methods

All animals were managed in accordance with the principles of laboratory animal care of the National Institutes of Health. In addition, all procedures were approved by the Institutional Animal Care and Use Committee of Taipei Veterans General Hospital.

Animal preparation and physiologic monitoring

Neonatal piglets, 3–4 weeks of age, were anesthetized with intramuscularly administered atropine (0.1 mg/dose) and ketamine (25 mg/kg/dose) prior to surgical procedures. All animals were placed in a supine position and given a subcutaneous injection of lidocaine hydrochloride (2%) for local anesthesia. After placing a 3.5-mm inside diameter uncuffed endotracheal tube (Murphy, Unomedical Sdn. Bhd., Kedah, Malaysia) via tracheotomy, controlled mechanical ventilation was established using a volume-controlled ventilator (Model 683; Harvard, South Natick, MA, USA). The tidal volume was set at 10 mL/kg, the ventilator rate at 40 breaths/minute, the inspiratory:expiratory ratio at 1:1, the positive end-expiratory pressure (PEEP) at 5 cmH₂O, and the fractional concentration of inspired oxygen (FiO₂) at 0.21 initially. After the induction of anesthesia, a solution of 0.33% sodium chloride in 5% dextrose was infused at a rate of 5 mL/kg/hr. Animals were then paralyzed with intravenous pancuronium bromide (0.2 mg/kg), sedated with midazolam (0.5 mg/kg), and maintained with a continuous infusion of ketamine (5 mg/kg/hr), midazolam (0.5 mg/kg/hr), and pancuronium bromide (0.2 mg/kg/hr). A 3.5-Fr umbilical vessel catheter (Argyle; Sherwood Medical Corp., Chicopee, MA, USA) was placed into the right femoral artery for continuous recording of arterial blood pressure and for arterial blood sampling. Another 3.5-Fr umbilical catheter was inserted into the left jugular vein for nutrition, anesthesia and central venous blood sampling. Body temperature was maintained at 38–39°C throughout the experiment with a servo-controlled heating blanket.¹⁸

Throughout the experiment, electrocardiography, arterial blood pressure, pulsative oxygen saturation (SpO₂) and body temperature were continuously monitored (Agilent M1205A, Philips Medical Systems, Andover, MA, USA).

NIRS

A pair of fiberoptic optodes was attached to the scalp of the animal with a probe holder after induction of anesthesia. The optodes were connected to the NIRS device (NIRO-100; Hamamatsu Photonics K.K., Hamamatsu City, Japan). The emitter and receiver were fixed in a probe holder to ensure an interoptode distance of 4 cm. rScO₂ was calculated from the differential signal obtained from the 2 sensors, expressed as a tissue oxygenation index (percentage of oxygenated hemoglobin = oxygenated hemoglobin / total hemoglobin [oxygenated hemoglobin + deoxygenated hemoglobin]).

Experimental protocol

Hypoxia experiments

To investigate the effects of hypoxia, 16 piglets were randomly assigned into 2 study groups: a hypoxia group ($n=8$) and a control group ($n=8$). In the hypoxia group, the hypoxic condition was induced by gradually decreasing the ventilator rate from 40 breaths/minute to 0 breaths/minute (with 5-breaths/minute decrements every 5 minutes) until the heart rate was <60 beats/minute. FiO₂ was kept at 0.21 during these procedures, which took about 40 minutes to complete. The ventilatory rate was then turned back to 40 breaths/minute, and FiO₂ was simultaneously increased to 1.0. After 40 minutes, FiO₂ was again turned to 0.21 for another 20 minutes. In the control group, piglets received a ventilatory rate of 40 breaths/minute during the entire experiment, with FiO₂ adjusted to 0.21 for the initial 40-minute period, 1.0 for the subsequent 40-minute period, and 0.21 for the final 20-minute period. The cardiopulmonary parameters were recorded every 5 minutes for a total of 100 minutes.

Resuscitation experiments

After completing the hypoxia procedure, all animals received intravenous injection of high-dose 15% potassium chloride until their hearts stopped beating. Animals from half of the hypoxia group and all of the control group were then divided into 3 groups with equal numbers to investigate the effects of resuscitation: a hypoxia-no CPR group ($n=4$), in which the first 4 animals from the previous hypoxia group were selected to receive no cardiopulmonary resuscitation (CPR); a control-no CPR group ($n=4$), selected from

the previous control group to receive no CPR; and a control-CPR group ($n=4$), in which the remaining 4 animals from the previous control group were selected to receive CPR for 30 minutes according to the standard procedures of the Neonatal Resuscitation Program (NRP), designed by the American Heart Association and the American Academy of Pediatrics.¹⁹ The ratio of ambu-bagging to chest compression was 1:3, with a total of 30 breaths ($\text{FiO}_2=1.0$) and 90 compressions per minute. All cardiopulmonary monitoring data were recorded every 5 minutes for 30 minutes in all 3 groups.

Arterial and central venous blood samples were taken every 5 minutes, and blood gas analysis calculating the values of SaO_2 , PaO_2 and PaCO_2 from arterial samples and SvO_2 , PvO_2 from venous samples was performed using an automatic blood gas system (STAT 3; NOVA Biomedical, Waltham, MA, USA). Measurement of rScO_2 was recorded at 5-minute intervals for 100 minutes before cardiac arrest, and at 1-minute intervals for 30 minutes after cardiac arrest. SpO_2 was recorded from pulse oximetry with a sensor placed on the foot of piglets (Agilent M1205A; Philips Medical Systems).

FTOE was calculated from rScO_2 and SaO_2 values.⁴ A ratio of $(\text{SaO}_2-\text{rScO}_2)/\text{SaO}_2$ was calculated to represent the balance between oxygen delivery and oxygen consumption. An increase in FTOE reflects an increase in oxygen extraction by the brain tissue, and a decrease in FTOE suggests that there is less utilization of oxygen by brain tissue, in relation to the supply of oxygen.⁴

Statistical analysis

All data were expressed as mean \pm SD. Results corresponding to the same parameters measured in 2 groups were compared by the unpaired t test method. The serial physiologic data of 2 groups at different time points were compared with 2-way repeated measures ANOVA, and followed by *post hoc* Student-Newman-Keuls' test for multiple pairwise comparison. Pearson's correlation coefficients were used to analyze correlations among rScO_2 , SaO_2 , SvO_2 , SpO_2 , PaO_2 and PvO_2 , and linear regression was used to analyze the linear relationship. Significance was accepted at the $p<0.05$ level.

Results

Mean body weight and age were 2.7 ± 0.3 kg and 14 ± 1 days in the hypoxia group, and 2.6 ± 0.3 kg and 14 ± 1 days in the control group, and there were no

significant differences between the groups. Baseline physiologic data did not vary significantly between the 2 study groups (Table 1).

Hypoxia experiments

The cardiopulmonary parameters and oxygen saturation at specific time points (20, 40, 60, 80, 100 minutes) are shown in Table 1. Significant hypoxia and hypercarbia were successfully induced by reducing the ventilatory rate in the hypoxia group at 20 and 40 minutes. Marked hypoxia, hypercarbia, acidosis, tachycardia and blood pressure changes in the hypoxia group were significantly different from those in the control group ($p<0.05$). The hypoxic animals regained their heart beats by 60 minutes after supporting ventilatory rate (40 breaths/minute) and 100% oxygen. Significantly higher PaO_2 and pH and lower PaCO_2 were observed at 60 minutes in the control group compared to the hypoxia group ($p<0.05$). However, only PaO_2 remained significantly higher in the control group 20 minutes later (Table 1). After stabilization, when FiO_2 was adjusted back to 0.21 after 80 minutes, there were no significant differences in gas exchange and cardiovascular parameters between the 2 study groups.

Changes in oxygen saturation parameters during the 100-minute observation period are displayed in Figure 1, and the values at specific time points are shown in Table 1. The changing (dropping) saturation patterns in rScO_2 , SvO_2 , SaO_2 and SpO_2 were similar, with decreasing ventilatory rate during the first 40 minutes in the hypoxia group. With the support of ventilation and 100% oxygen, there was a marked increase in all oxygen saturation parameters. A short and marked rebound phenomenon in rScO_2 was observed in the hypoxia group compared to the control group, when a significantly higher rScO_2 was noted 5 minutes later; rScO_2 subsequently returned to levels that were not significantly different between groups. At the end of the experiment, when FiO_2 was turned back to 0.21, the rScO_2 of the hypoxia group was significantly lower than that of the control group. However, there were no significant differences in SvO_2 and SaO_2 between the 2 study groups after the 40-minute time point.

The changes in FTOE during the 100-minute observation period are presented in Figure 2. The FTOE values in the hypoxia group gradually dropped along with the hypoxic conditions, and then gradually increased when the re-oxygenation process was performed. Beginning at the 60-minute time point and persisting until the end of the experiment, there was a tendency toward higher FTOE values in the hypoxia group compared to the control group (Figure 2).

Table 1. Serial physiologic data and oxygenation parameters in experimental animals in the hypoxia and control groups

Situation	Baseline	Changing ventilatory rate			High oxygen supply		Original setting
Time (min)	0	20	40	60	80	100	
FiO ₂	0.21	0.21	0.21	1.0	1.0	0.21	
Hypoxia group (n = 8)							
Ventilatory rate (/min)	40	20	0	40	40	40	
Heart rate (beats/min)	190 ± 30	207 ± 43	55 ± 4 ^{bc}	206 ± 32 ^d	225 ± 48 ^d	253 ± 53 ^{bd}	
MBP (mmHg)	92 ± 10	109 ± 20	31 ± 1 ^{bc}	90 ± 6 ^d	93 ± 9 ^d	95 ± 27 ^d	
pH	7.41 ± 0.06	7.30 ± 0.07 ^b	6.97 ± 0.16 ^{bc}	7.26 ± 0.1 ^{bd}	7.34 ± 0.07 ^{bd}	7.33 ± 0.14 ^{bd}	
PaCO ₂ (mmHg)	33 ± 6	47 ± 6 ^b	78 ± 24 ^{bc}	40 ± 5 ^{cd}	33 ± 5 ^{cd}	34 ± 4 ^{cd}	
PaO ₂ (mmHg)	78 ± 8	46 ± 14	21 ± 5	266 ± 111 ^{bcd}	280 ± 93 ^{bcd}	52 ± 10 ^{ef}	
PvO ₂ (mmHg)	40 ± 5	29 ± 7 ^b	18 ± 3 ^{bc}	56 ± 8 ^{bcd}	48 ± 8 ^{bcd}	29 ± 7 ^{bdef}	
rScO ₂ (%)	49 ± 3	38 ± 8 ^b	18 ± 7 ^{bc}	51 ± 5 ^{cd}	48 ± 4 ^{cd}	38 ± 4 ^{bdef}	
SvO ₂ (%)	75 ± 4	46 ± 18 ^b	12 ± 6 ^{bc}	81 ± 6 ^{cd}	78 ± 8 ^{cd}	46 ± 21 ^{bdef}	
SaO ₂ (%)	95 ± 2	71 ± 14 ^b	19 ± 1 ^{bc}	100 ± 0 ^{bd}	100 ± 0 ^{bd}	83 ± 6 ^{bdef}	
SpO ₂ (%)	96 ± 5	62 ± 23 ^b	UD	100 ± 0 ^c	100 ± 0 ^c	77 ± 12 ^{bcef}	
Control group (n = 8)							
Ventilatory rate (/min)	40	40	40	40	40	40	
Heart rate (beats/min)*	169 ± 28	181 ± 33	196 ± 48 ^a	191 ± 46	201 ± 41	227 ± 43	
MBP (mmHg)*	79 ± 21	81 ± 21 ^a	87 ± 26 ^a	84 ± 27	91 ± 26	98 ± 18	
pH*	7.41 ± 0.05	7.41 ± 0.05 ^a	7.39 ± 0.06 ^a	7.39 ± 0.05 ^a	7.37 ± 0.05	7.36 ± 0.06	
PaCO ₂ (mmHg)*	32 ± 4	32 ± 2 ^a	32 ± 4 ^a	31 ± 4 ^a	34 ± 5	33 ± 5	
PaO ₂ (mmHg)*	80 ± 14	74 ± 17	68 ± 16	380 ± 44 ^{abcd}	377 ± 73 ^{abcd}	63 ± 14 ^{ef}	
PvO ₂ (mmHg)*	47 ± 10	42 ± 2 ^a	40 ± 6 ^a	61 ± 6 ^{bcd}	61 ± 6 ^{bcd}	38 ± 8 ^{ef}	
rScO ₂ (%)*	48 ± 3	46 ± 4 ^a	45 ± 4 ^a	52 ± 3 ^d	52 ± 4 ^{ad}	43 ± 3 ^{aef}	
SvO ₂ (%)*	79 ± 8	76 ± 5 ^a	72 ± 10 ^a	87 ± 6 ^d	86 ± 7 ^d	63 ± 15 ^{ef}	
SaO ₂ (%)*	95 ± 3	93 ± 5 ^a	91 ± 6 ^a	100 ± 0 ^d	100 ± 0 ^d	89 ± 7 ^{ef}	
SpO ₂ (%)*	96 ± 4	93 ± 8 ^a	88 ± 11 ^a	100 ± 0	100 ± 0	83 ± 13 ^{bef}	

* $p < 0.05$ vs. hypoxic group, analyzed by 2-way repeated measures ANOVA as a function of group and time; ^a $p < 0.05$ vs. corresponding data at the same time point of the hypoxia group; ^b $p < 0.05$ vs. corresponding data of 0 minutes in the same group and parameter; ^c $p < 0.05$ vs. data of 20 minutes in the same group and parameter; ^d $p < 0.05$ vs. data of 40 minutes in the same group and parameter; ^e $p < 0.05$ vs. data of 60 minutes in the same group and parameter; ^f $p < 0.05$ vs. data of 80 minutes in the same group and parameter. FiO₂ = fractional concentration of inspired oxygen; rScO₂ = regional cerebral tissue oxygen saturation; SaO₂ = arterial oxygen saturation; SpO₂ = pulse oxygen saturation; SvO₂ = jugular venous oxygen saturation; MBP = mean arterial blood pressure; PaO₂ = arterial oxygen tension; PvO₂ = jugular venous oxygen tension; PaCO₂ = arterial carbon dioxide tension.

Resuscitation experiments

There were no significant differences among the 3 study groups in cardiopulmonary parameters before injection of high-dose potassium chloride. The arterial blood gas changes during the resuscitation study are shown in Figure 3. Significantly higher PaO₂ and lower PaCO₂ values were observed in the control-CPR group compared to the other groups. However, there were no significant differences in arterial pH. Figure 4 shows the serial changes in rScO₂ and FTOE in these post-cardiac arrest animals. A rapid drop in rScO₂ during the 1st minute was noted in all 3 groups. By 2 minutes after cardiac arrest, rScO₂ had dropped to its lowest value (around 31%), and then began slightly increasing to approximately 35% in all groups. Although aggressive resuscitation was performed in the control-CPR group, there was no significant difference in rScO₂ during the 30-minute post-cardiac arrest period (Figure 4A).

However, FTOE was maintained in the control-CPR group while it dropped in the other 2 groups. Significant differences in FTOE values between groups were observed between 20–30 minutes after cardiac arrest (Figure 4B).

The correlations between rScO₂ and other oxygenation parameters were analyzed and are presented in Figure 5. There were significantly positive and linear correlations between rScO₂ and SvO₂ ($r = 0.846$, $p < 0.001$), PvO₂ ($r = 0.809$, $p < 0.001$), SaO₂ ($r = 0.842$, $p < 0.001$) and SpO₂ ($r = 0.831$, $p < 0.001$).

Discussion

Our study demonstrated the influence of hypoxia and the effects of CPR on regional brain tissue oxygenation. The responses in rScO₂ were faster than FTOE

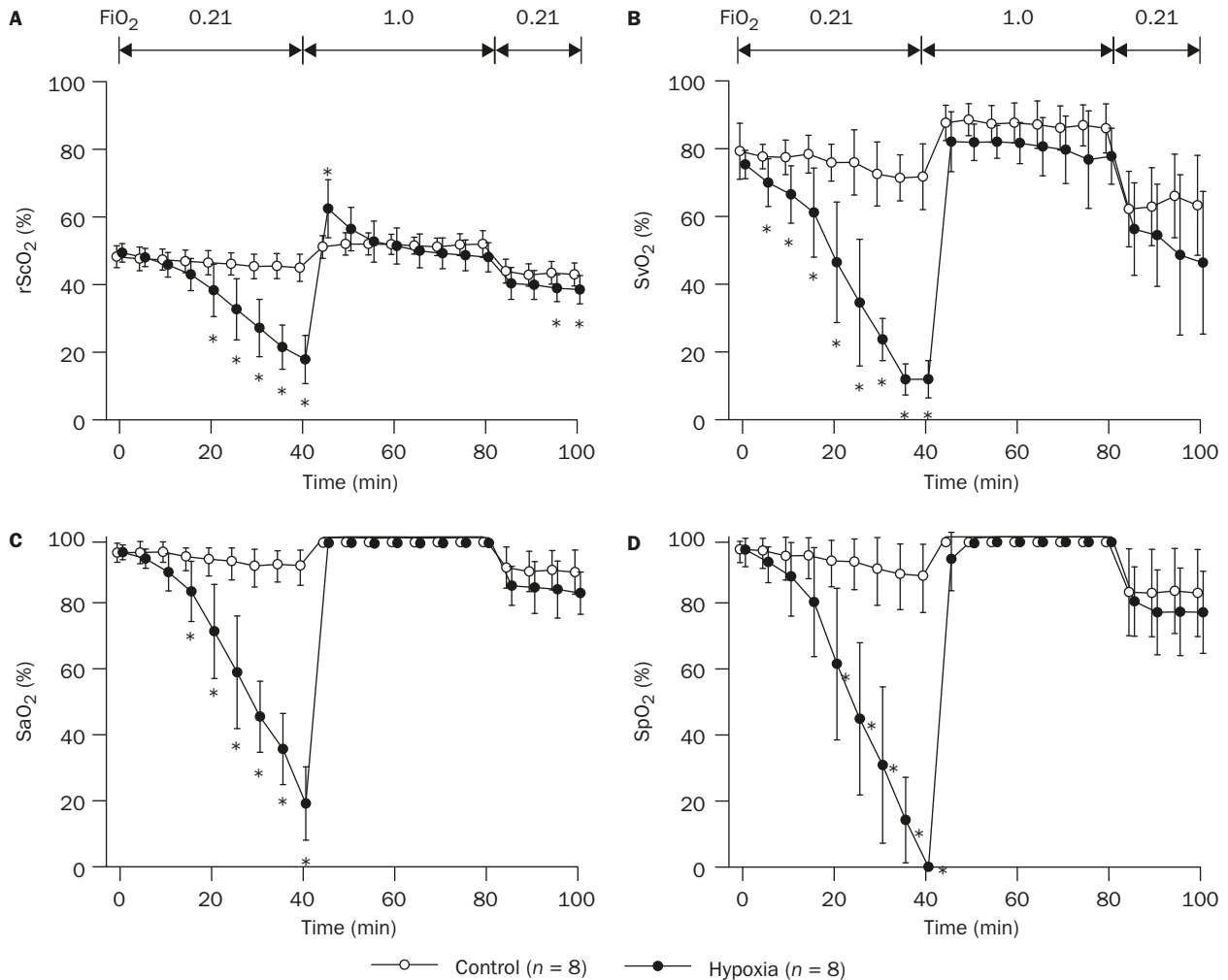


Figure 1. Changes in the oxygenation saturation parameters of the hypoxia and control groups. (A) Regional cerebral tissue oxygen saturation (rScO₂). (B) Jugular venous oxygen saturation (SvO₂). (C) Arterial oxygen saturation (SaO₂). (D) Pulse oxygen saturation (SpO₂). FiO₂ = fractional concentration of inspired oxygen. **p* < 0.05 vs. corresponding data of the control group at the same time point.

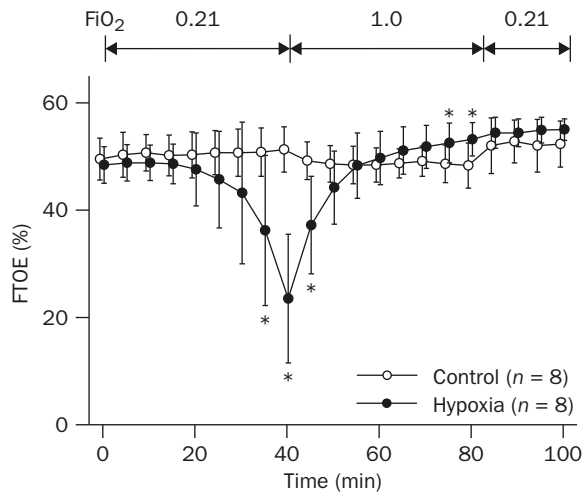


Figure 2. Changes in fractional cerebral tissue oxygen extraction (FTOE) in hypoxia and control groups. **p* < 0.05 vs. corresponding data of the control group at the same time point.

during the hypoxic and re-oxygenated conditions. Also, FTOE could be maintained in the cardiac arrest animals by effective CPR, and that was not demonstrated in rScO₂.

In the field of neonatal intensive care, hypoxic events caused by a variety of factors result in common clinical conditions. After oxygen and ventilation support, or after a standard CPR procedure, most cardiovascular conditions can be regained;^{20,21} however, brain damage may occur in some instances. Detection of cerebral hypoxic-ischemic events remains problematic in neonates because findings from neurologic examination, cerebral blood flow (CBF) measurements, and jugular venous saturation monitoring are unreliable or impractical. NIRS has been evaluated as a potentially useful method to measure CBF and other parameters.²² Other studies using NIRS in neonates at risk of hypoxic-ischemic brain damage have demonstrated

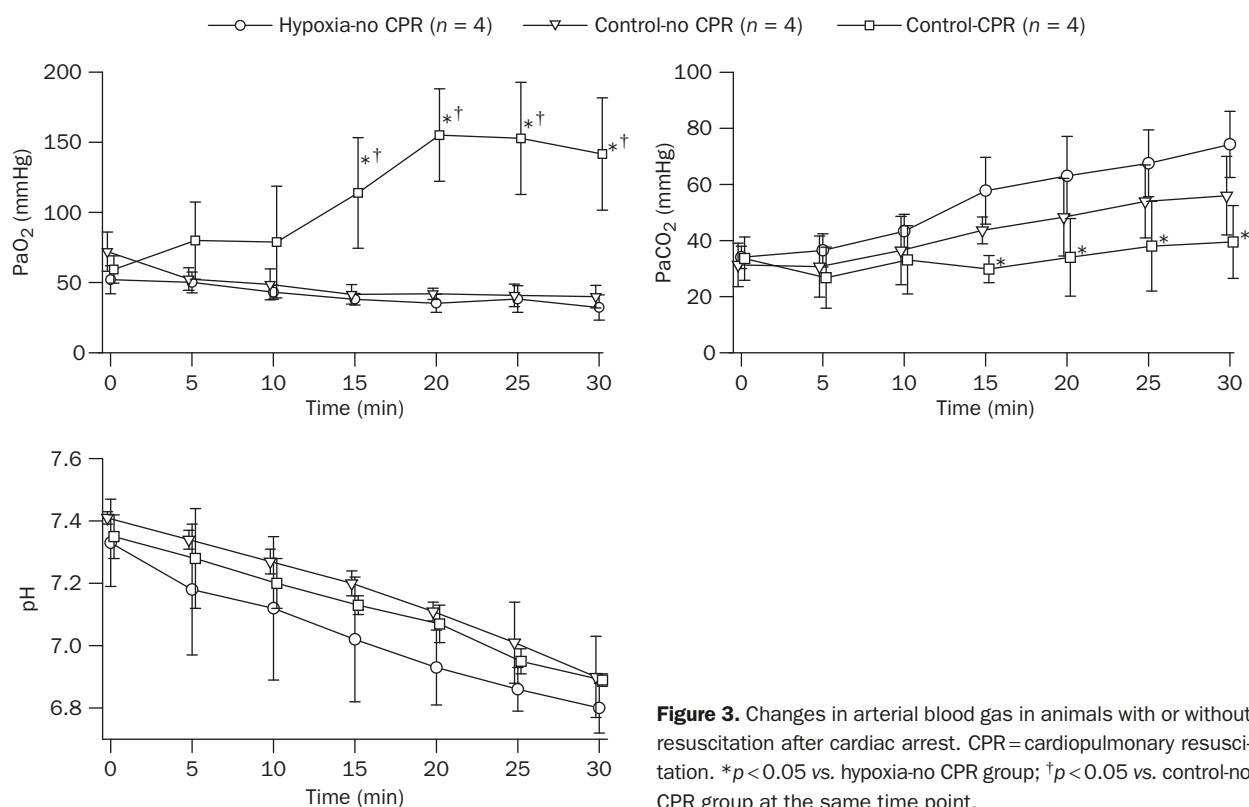


Figure 3. Changes in arterial blood gas in animals with or without resuscitation after cardiac arrest. CPR=cardiopulmonary resuscitation. * $p < 0.05$ vs. hypoxia-no CPR group; † $p < 0.05$ vs. control-no CPR group at the same time point.

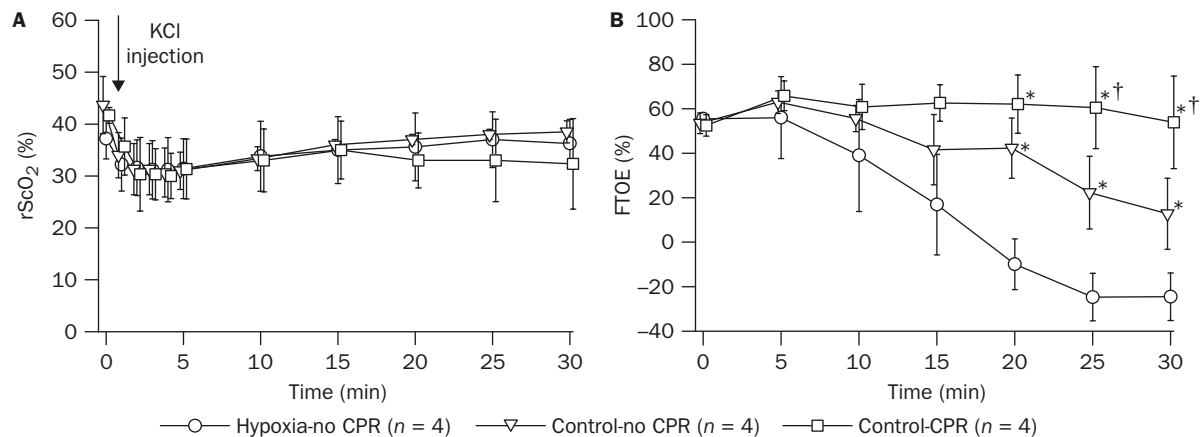


Figure 4. Changes in regional cerebral tissue oxygen saturation (rScO₂) and fractional cerebral tissue oxygen extraction (FTOE) in animals with or without resuscitation after cardiac arrest. (A) Changes in rScO₂; there was no significant difference among groups. (B) Changes in FTOE. * $p < 0.05$ vs. hypoxia-no CPR group; † $p < 0.05$ vs. control-no CPR group at the same time point.

episodes of decreased cerebral hemoglobin oxygenation.^{12–15,17} Huang et al reported lower rScO₂ in neonates with hypoxic-ischemic encephalopathy than was seen in healthy neonates.²³ Furthermore, Kurth et al found that as CBF and jugular venous saturation decreased, functional activities of the brain became impaired and presented with low rScO₂.⁷ However, Toet et al used FTOE to calculate oxygen extraction

by brain tissue, and found that decreased FTOE and increased rScO₂ observed after 24 hours of age in neonates with hypoxic-ischemic episodes at delivery correlated with adverse outcome.⁴ Therefore, FTOE should be taken into consideration when evaluating rScO₂ data. Our study focused on both rScO₂ and FTOE.

During the hypoxia experiment, simultaneous decreases in all oxygenation parameter values were due

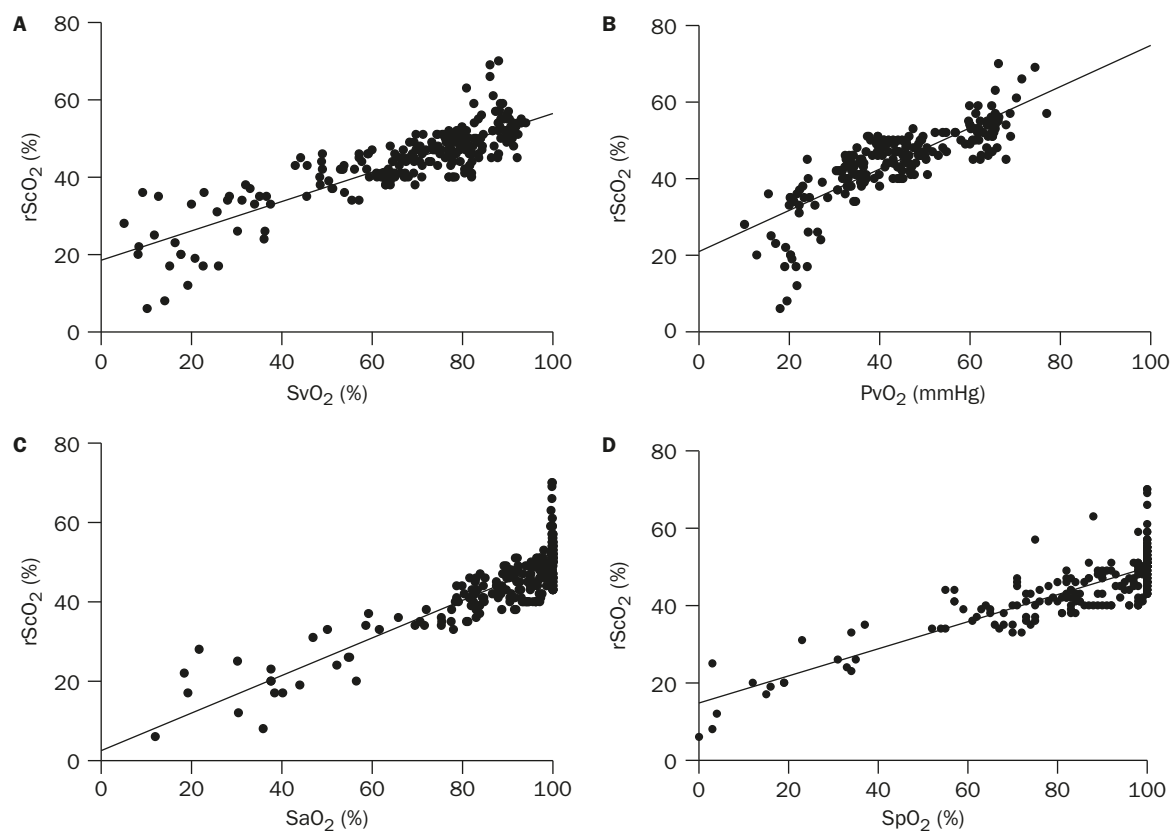


Figure 5. Correlations among different oxygenation parameters. There was significantly linear correlation between $rScO_2$ and each one of SvO_2 , PvO_2 , SaO_2 , and SpO_2 . Regression equations are as follows: (A) $rScO_2 = 18.900 + 0.374x SvO_2$, $r^2 = 0.716$, $p < 0.001$; (B) $rScO_2 = 20.973 + 0.538x PvO_2$, $r^2 = 0.654$, $p < 0.001$; (C) $rScO_2 = 4.874 + 0.448x SaO_2$, $r^2 = 0.708$, $p < 0.001$; (D) $rScO_2 = 14.791 + 0.350x SpO_2$, $r^2 = 0.691$, $p < 0.001$. PvO_2 =venous oxygen tension; $rScO_2$ =regional cerebral tissue oxygen saturation; SaO_2 =arterial oxygen saturation; SpO_2 =pulse oxygen saturation; SvO_2 =jugular venous oxygen saturation.

to gradually decreasing ventilator rate that induced hypoxemia, hypercapnea and acidosis in experimental piglets. The design of hypoventilation mechanism in this study protocol was based on the common clinical conditions of sick neonates with apnea or poor respiratory function. The transient overshoot of $rScO_2$ during re-oxygenation in the hypoxia group is possibly explained by the slow CBF induced by the hypoxic condition, which resulted in a transient greater release of oxygen from the blood than is normally supplied to the cell during the initial re-oxygenation period, and which also helps to increase the FTOE. However, when fully saturated with oxygen, animals regained new equilibrium conditions, with a tendency toward lower $rScO_2$ and higher FTOE in the hypoxia group than in the control group. This phenomenon may indicate some kind of brain tissue injury during the short hypoxic period.

During the resuscitation experiments, effective oxygenation and ventilation were achieved by CPR; however, profound acidosis was observed in all 3 groups.

The acidosis may have influenced the CBF, which further influenced the resulting $rScO_2$. This may explain why there were no differences in $rScO_2$ among study groups. Corrections of the metabolic acidosis may further improve CBF, and possibly further improve outcome in cardiac arrest conditions. Additional studies will be necessary to elucidate this issue. In addition, the $rScO_2$ dropped to its lowest limit at 2–5 minutes after cardiac arrest, which may have reflected severe reductions in CBF that caused functional impairment and further structural damage of the brain cells. Slight rebound of $rScO_2$ values during 15–30 minutes after cardiac arrest may have been due to decreased body temperature resulting from the decreased cerebral oxygen metabolic rate and blood circulation. When the decrease in cerebral oxygen supply is smaller than the decrease in its consumption, $rScO_2$ may increase. The gradually decreased FTOE in the 2 groups without CPR demonstrated a decreased extraction and consumption of cerebral oxygen. Furthermore, the differences in FTOE in the 2 groups with no CPR indicate

the possibility of functional damage during previous hypoxic conditions in the hypoxia-no CPR group.

NIRS measures the oxygenation state in the underlying tissue and reflects a mixture of intravascular oxygenated and deoxygenated venous, arterial and capillary hemoglobin. This is especially true for the venous portion, which predominately determines NIRS measurement of cerebral oxygenation.^{24,25} Investigations of the relationship between jugular bulb oxygen saturation and regional cerebral oxygenation measured by NIRS have obtained different results.^{24–28} Daubeney et al demonstrated a good correlation between jugular venous oxygen saturation and rScO₂ during heart catheterization and cardiac surgery in children with congenital heart diseases.²⁶ Weiss et al showed that the presence of intracardiac shunt and extracerebral tissue (bone and scalp) affected rScO₂ measurement; without these impediments to blood sampling from the right atrium, better correlation could be found between rScO₂ and central venous saturation.²⁵ In our study, the SvO₂ was measured from the left jugular vein and represented jugular venous saturation. Significantly positive correlations were demonstrated between noninvasive rScO₂ and other oxygen saturation parameters, including invasive SvO₂, SaO₂ and noninvasive SpO₂. Therefore, similar to previous reports,^{7,23} low rScO₂ was predictable during hypoxia when vascular hemoglobin deoxygenation was caused by hypoxia.

FTOE has been used to investigate the balance between oxygen delivery and oxygen consumption.⁴ An increase in FTOE reflected an increase in oxygen extraction by brain tissue, which suggested a higher oxygen consumption in relation to oxygen delivery.⁴ Thus, when the brain tissue survives and remains active, FTOE should not be low. When brain tissue has been damaged or is dying, low FTOE could be predicted. Therefore, FTOE may be more reliable when evaluating patients with brain damage. Our experimental findings and the clinical findings of Toet et al both support the observations on FTOE.⁴

Although noninvasive monitoring of SpO₂ is conveniently and commonly used in clinical practice, SpO₂ may not be easily detectable when the patient's condition is unstable, especially when the blood pressure is low or undetectable. In our CPR experiment, rScO₂ was detected in all groups. However, SpO₂ was only detected in animals that received effective cardiac massage. This is because the signal for SpO₂ depends on small artery pulsation, a parameter used to indicate systemic circulation and not regional tissue oxygenation. Therefore, regional tissue oxygenation detected by noninvasive NIRS is more reliable than SpO₂ in hemodynamically unstable conditions.²³

In conclusion, hypoxic events and cardiac arrest decrease brain tissue oxygenation and oxygen extraction. Effective resuscitation helps to maintain brain tissue viability, and that can be detected by monitoring rScO₂ and calculating FTOE. Therefore, noninvasive monitoring of rScO₂ and evaluating FTOE changes may help clinicians to evaluate brain tissue oxygenation and viability in critical newborns with hypoxia or receiving resuscitation.

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